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ESTIMATION OF ALCOHOL IN CONCENTRATED NITROUS ETHER.

By W. A. Pearson.

In searching for an accurate method for determining alcohol in concentrated nitrous ether, I tried the method described by Dupré (Allen, Vol. I, page 102 and *J.A.C.S.*, Vol. XX, page 495) and found it to be very accurate for dilute alcoholic solutions containing from 0·1 gramme to 0·3 gramme in 20 c.c. The accuracy was tried on dilute solutions of alcohol of known strength, the results of analyses differing from the actual amount of alcohol present by only one or two units in the second decimal place, if proper conditions are observed.

The next step was to separate the alcohol from the nitrous ether. Various methods were tried, with varying success, but the evaporation of the concentrated nitrous ether in a flask containing water, and passing the vapor through water seemed advantageous. At first a small Erlenmeyer flask about one-fourth full of ice-water was weighed accurately, 20 to 35 grammes of concentrated nitrous ether poured in, and again accurately weighed. Anticipating your objections to direct weighing of so volatile a liquid under these conditions, will say that only a very slight error will be made if flask and concentrated nitrous ether are very cold and having the subsequent apparatus near the scales, ready to be connected with the flask. The proper weights are placed on the scales slightly below the correct weight of flask, ice-water and concentrated nitrous ether, and as the weight changes, at the proper moment remove the flask from scales and connect at once with the apparatus.

If this method be carefully followed not more than 1 milligramme

will be lost, and the error is not large because only from 10 to 20 per cent. of this is alcohol.

Various forms of apparatus were used, at first merely connecting with upright condensers and allowing the nitrous ether to evaporate

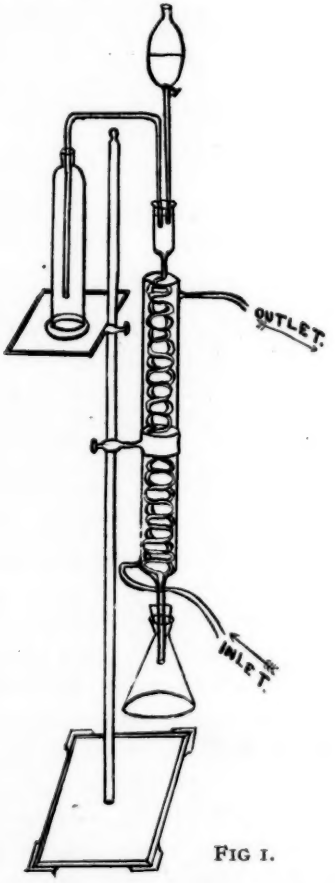


FIG 1.

at room temperature; later a modification of this method was adopted, which works quite satisfactorily. The flask is connected with an upright spiral condenser and in the top is poured ice-water. If the lower opening is quite small, a spiral column of ice-water will be held in the condenser by the pressure developed by the volatilizing concentrated nitrous ether, and will necessitate each bubble of gas passing through this spiral column of cold water. (Fig. 1.)

Another form by which I obtained good results consisted of a bulb thistle tube connected at the top by a large glass spiral and at the bottom by the flask containing the nitrous ether. Water was placed in the spiral in such a way that it remained at the bottom of each turn; water was also placed in the bulbs of the thistle tube. (Fig. 2.)

The later apparatus used was merely a series of five tall wash-bottles, three-quarters filled with water, with the outlet of each bottle reaching nearly to the bottom of the next bottle. This form has simplicity as its chief advantage, and also temperature conditions can be carefully controlled.

In any of the above apparatus at least three days should be allowed for the evaporation of the concentrated nitrous ether.

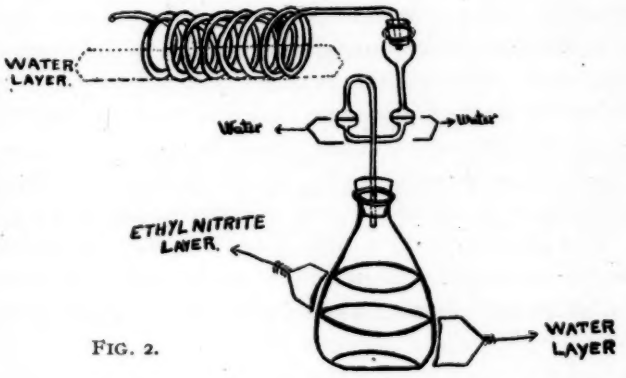


FIG. 2.

When volatilization is complete, the water in the apparatus is combined and put in a measuring flask of such size that, when diluted, 20 c.c. of it will contain from 0·1 gramme to 0·3 gramme of alcohol. The apparatus is carefully washed with ice-water, and washings added to measuring flask, making the proper volume.

After mixing well the combined washings and dilute solution of alcohol from the apparatus, 20 c.c. are accurately measured into a clean magnesium citrate bottle which can easily be obtained with a tight stopper. This solution contains the alcohol and some nitrous ether, depending on the form of apparatus used and the rate of volatilization. The proper amount of oxidizing agent must now be added to destroy the nitrous ether and 10 c.c. more of the chromic acid mixture added to change the alcohol pres-

ent into acetic acid. Potassium permanganate, either solid or in solution, may be added to destroy the nitrous ether and has the advantage of roughly showing the amount of nitrous ether present. Potassium iodide with sulphuric acid cannot be used to destroy the nitrous ether, owing to later volatilization of the iodine.

It is well to titrate a portion with tenth normal potassium permanganate, to form an idea of the amount of nitrous ether present. I prefer to do this and then use sufficient chromic acid mixture to both destroy the nitrous ether and convert the alcohol, as potassium permanganate leaves a muddy residue. One or two trials may be necessary to determine the exact quantity to be used. After the addition of the chromic acid, the bottle is firmly closed and heated for two hours in a steam-bath at 100° C. At the end of this time the solution should not be green, but should have a small excess of chromic acid. The bottle must now be cooled to room temperature, opened, and a small piece of metallic zinc added to destroy the excess of chromic acid; when solution is green, it is poured into a distilling flask, the bottle washed into same flask and carefully distilled, using a well-cooled condenser. When liquid in distilling flask is nearly to dryness, add more water and again distil almost to dryness. If last few drops of distillate are acid to litmus paper, again refill and distil. Test distillate with a drop of barium chloride solution to be positive no sulphuric acid has been carried over, and titrate with standard alkali and compute alcohol present in original sample.

ANALYTICAL RESULTS.

Using flask connected with thistle tube and air-cooled glass spiral, the following results were obtained:

No.		Per cent.
1.	Using KI and H_2SO_4 to destroy nitrous ether present, alcohol indicated	6.11
2.	" $KMnO_4$ " " " " " " " "	11.73
3.	" chromic acid " " " " " " " "	14.53
4.	" " " " " " " " " " " "	15.30
5.	" " " " " " " " " " " "	15.02

Using series of five wash-bottles with different amounts of dilute alcohol and chromic acid and on different days, the following results were obtained:

No.	Date	Alc. Sol.	Chromic acid mixture	Standard Alkali required	Per cent. of alcohol in original
1.	December 24	20 c.c.	20 c.c.	7·4 c.c. normal	16·5
2.	" 24	20 c.c.	20 c.c.	Bottle broken in steam-bath	
3.	" 24	20 c.c.	15 c.c.	7·5 c.c. normal	16·7
4.	" 24	15 c.c.	20 c.c.	5·5 c.c. "	16·4
5.	" 24	10 c.c.	12 c.c.	3·7 c.c. "	16·5
6.	" 24	10 c.c.	13 c.c.	3·7 c.c. "	16·5
7.	" 26	20 c.c.	23 c.c.	7·2 c.c. "	16·0
8.	" 26	20 c.c.	23 c.c.	7·35 c.c. "	16·3
9.	" 26	15 c.c.	18 c.c.	55·1 c.c. " tenth	16·4
10.	" 26	15 c.c.	18 c.c.	54·4 c.c. " "	16·2
	Average				16·44

A 4·8376 gramme sample of the original nitrous ether was weighed in a cold 100 c.c. flask, diluted at once to 100 c c. with alcohol, and tested in nitrometer for absolute ethyl nitrite.

No.		
1.	5 c.c. of this solution liberated	65 c.c. of nitric oxide
2.	5 c.c. " " " "	65·2 c.c. " " "
	Average	65·1 c.c.

65·1 c.c. of nitric oxide represents 82 63 per cent. of absolute ethyl nitrite in sample. The indicated composition of this sample is, therefore: alcohol, 16·44 per cent., ethyl nitrite, 82·63 per cent.

SUMMARY.

Alcohol can be estimated in concentrated nitrous ether by the method of Dupré, using certain modifications, as outlined. The experimental error is large, unless exceptional care is taken at every step, because the final error is magnified by multiplication in computation. Aldehydes, if they be present, will be estimated along with alcohol, and some of the methods for estimating aldehydes must be used for this correction. In the samples above examined no aldehyde was detected by addition of ammonia or solution of sodium bisulphite. Reduction tests for aldehydes, of course, are useless in the presence of ethyl nitrite.

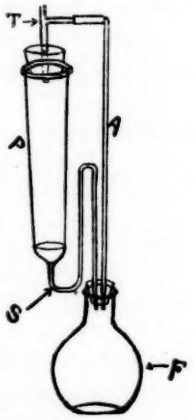
Any ethyl nitrite left dissolved in the water along with the alcohol is also changed into acetic acid. This error is so slight that it may, in most cases, be ignored. A correction may be subtracted for this error by estimating the amount of ethyl nitrite in the water by means of a nitrometer.

From Research Laboratory of
Smith, Kline & French Company.

MODIFICATION OF THE SOXHLET EXTRACTOR.

By Horatio C. Wood, Jr.,
Associate Professor of Pharmacology, University of Pennsylvania.

The apparatus here shown for continuous extraction by volatile solvents has proven itself efficient and offers certain advantages over the Soxhlet extractor, notably in its simplicity and inexpensiveness. It consists of a narrow percolator (P) the lower end of which is connected by means of a tightly fitting cork with a siphon-shaped glass tube, and the upper end closed with a perforated cork into which is fitted a glass "T" tube. The rectangular limb of this tube is connected by a very short piece of rubber with a glass tube



Modified Soxhlet Extractor.

bent at right angles which passes down to the flask containing the solvent. When the contents in the flask (F) are boiled, the vapors pass up through the tube (A) into the tube (T); the upper end of (T) is connected with a reflux cooler into which the vapors pass and, being condensed, run down into the percolator (P) and thence back through (S) into the flask.

Besides the advantages over the Soxhlet apparatus of being less expensive and much less fragile, the facts that by simply removing the corks in each end of the percolator, the apparatus can be easily and quickly cleaned, and that by simply substituting different sizes of percolators it can be adapted for either large or small quantities of drugs with comparatively little trouble, have persuaded me to describe it.

DOES DIGITOXIN REPRESENT THE THERAPEUTIC VIRTUES OF DIGITALIS?

By Horatio C. Wood, Jr.

Associate Professor of Pharmacology, University of Pennsylvania.

Within the last year or two there has been a revival of the idea that was prevalent a generation ago that digitoxin might be regarded as the active principle of digitalis. In 1871 Nativelle was awarded the Orfila prize for the discovery of the active principle of digitalis. Although he named his substance digitaline—under which title it is still recognized by the French Codex—it is generally regarded as identical with the substance described by Schmiedeberg as digitoxin. This discovery attracted much attention, and naturally the crystalline principle enjoyed for a time considerable popularity. It failed, however, to sustain its place as a practical remedy, and its use outside of France was almost entirely abandoned. Recently, however, largely on account of vigorous advertising by certain drug manufacturers, digitoxin has again come to the fore as representing the therapeutic properties of digitalis in a compact and pure form. There are certain observations which would seem to throw some doubt on the justice of this claim.

In the first place, attention may be called to the small amount of digitoxin found in digitalis leaves in comparison to the relative toxicity of the crude drug and of the glucoside. While it is true that digitoxin is the most actively poisonous of the principles which have so far been discovered in digitalis, it seems well established that the dose required to influence the circulation is disproportionately large when compared to the amount contained in the leaves. Digitalis is a drug showing such great variations in potency that it is difficult to draw accurate conclusions concerning the comparative physiological activity of the digitalis leaves without a simultaneous chemical and physiological study of the same individual specimen of the drug. The proper method to arrive at the conclusion concerning the quantitative action of an active principle would be to take a specimen of the crude drug, determine by chemical assay the proportion of principle present, determine by physiological experiment the dose of the crude drug required to kill, also the dose of the principle required to kill, and if the principle accurately

represented the drug, then the fatal dose of the principle should correspond to the amount chemically found in the single dose of the crude drug. Unfortunately, as far as I know, there has been no such study made of digitalis, and we have to rely upon more or less indirect evidence. For instance, in the research carried out some years ago (*Amer. Journ. Medical Sciences*, August, 1900) by Dr. Arnold and myself we found that the average dose of digitalis immediately fatal was, for a dog, 0·15 gramme per kilo of body weight, and that the fatal dose of Merck's digitoxin was about 3 milligrammes per kilo. The average content of digitalis leaves in digitoxin would seem to be, from various reports, between 0·15 and 0·3 of 1 per cent.; if we allow 0·2 per cent. as an average, in the fatal dose of digitalis for a dog there would be contained but 0·3 milligramme, or about one-tenth of the quantity of digitoxin required to kill. These figures, for the reasons just mentioned, would not in themselves be convincing, but they find confirmation in clinical experience which makes them very suggestive. From the reports of a considerable number of authors it would seem that from clinical experience 0·5 milligramme may be regarded as the average therapeutic dose of digitoxin[1] corresponding to the effects of 0·06 gramme of digitalis leaves. This quantity of digitalis leaves, however, would contain but 0·12 milligramme, so that while the discrepancy is not quite so great as in our experiments, there is still a difference of more than 400 per cent. to be accounted for.

It would seem evident, therefore, that digitoxin does not represent in activity more than one-fourth of the power of digitalis, and any assay process of digitalis based upon the quantity of digitoxin it contains, discards three-fourths of the active substance of the plant. As rational would it be, apparently, to assay opium for the codeine in it, neglecting the morphine, as to assay digitalis for its digitoxin alone.

If digitoxin possesses the precise physiological and therapeutic properties of digitalis leaf, the mere quantitative difference becomes a matter of minor importance, since it only necessitates the giving of a comparatively large amount. But this does not, from our present knowledge, seem to be the case. One of the most interesting re-

[1] See Wenzel (*Therap. Monatsch.*, 1895, ix), Von Starck (*Ibid.*), Masius (*Bull. Acad. Roy. Belg.*, 1893, vii), Curioni (*Clin. Med. Ital.*, 1901), etc.

searches bearing on this point is that of Fraenkel (*Archiv. für Exper. Path. und Pharm.*, Vol. li, p. 84). This observer found that after the administration of minimum lethal doses of digitoxin no slowing of the pulse occurred for from twelve to twenty-four hours, but when the effect of the drug began, it passed through the therapeutic stage into poisoning and even death. He found that it was well-nigh impossible to produce from a single dose of digitoxin any therapeutic slowing of the pulse which was not followed later by toxic manifestations; in other words, the border-line between the therapeutic dose and the poisonous dose was so extremely narrow that no one could walk therein. By the administration, however, of comparatively small doses for several days, he could produce easily a marked slowing of the pulse. But here again the peculiar persistency and tendency to show a cumulative effect of digitoxin above the other principles became manifest. For instance, whereas, he could continue administering one-half of the lethal dose of digitalin daily for many weeks without toxic symptoms, one-third of the fatal dose of digitoxin repeated daily for three days caused violent poisoning.

Again, as before, these results have been confirmed by clinical experience. Hatcher (*Jour. Amer. Med. Assoc.*, Vol. xlvii, p. 2059) says, in speaking of digitoxin: "Among these disadvantages are: its insolubility in water and consequent irritant action, slowness to act, and tendency to cumulative effect; its proneness to decomposition, whereby toxiresin is formed; the narrow margin between the effective dose and that which causes cumulative effects on continued use; and its marked vaso-constrictor effects, which may or may not be objectionable, dependent on the case in hand. . . . This insolubility also seems to be responsible for the delay of forty-eight hours or more in inducing the cardiac effects."

For the above reasons it would seem extremely doubtful that digitoxin represents digitalis either quantitatively or qualitatively; for while in a general way the effects of digitoxin upon the circulation are similar to those of digitalis, there are certain differences which may seem slight, but yet which are of great practical importance. Kakowski (*Archiv. Internat. die Pharmac. und die Therap.*), in a series of studies upon the isolated heart of both the frog and the mammal, reached the conclusion that none of the principles thus far found in digitalis had the same effect upon the heart muscle as did the tincture or infusion of digitalis. The principles he studied included digitoxin, digitalein and digitalinum.

In closing, I quote, as having some bearing on the question of the practical utility of digitoxin, from Dixon (*Manual of Pharmacology*, 1906, p. 169): "The samples of digitoxin at present on the market vary in activity even more than the galenical preparations."

THE STANDARDIZATION OF PREPARATIONS OF DIGITALIS BY PHYSIOLOGICAL AND CHEMICAL MEANS.

I. BY PHYSIOLOGICAL MEANS.

BY DR. E. D. REED.

The question of the physiological standardization of drugs is one that has been attended by a great deal of interest both by pharmaceutical chemists and physicians. No one can deny the desirability and the value of knowing the exact physiological activity of any preparation to be used as a medicine. However, the methods commonly employed for physiological testing are by no means accepted by everyone as correct, or as showing the real activity of a drug.

Without doubt, wherever a chemical assay is possible, it forms the most reliable means of anticipating the physiological or therapeutic activity of any given preparation. This, however, does not rule out the desirability of a control test by physiological methods; but whether or not this should be carried out in all instances is a question hard to decide.

Perhaps no drug has received a greater amount of attention in an effort to formulate a reliable method for standardization than digitalis and other members of the so-called digitalis series.

It is not necessary to consider the other members, such as strophanthus, hellebore, squill, etc., as digitalis is the most important member of this series. The isolation of the active principles of digitalis is rather difficult, and it has been maintained by a number of very competent observers that a chemical assay of digitalis and its preparations is of little value in estimating the physiological activity of the drug. Digitalis and the other members of this family are noted for their stimulating action upon the heart. A great many other properties, namely diuretic, and action on the central nervous system, have been claimed for digitalis, and several attempts have been made to show that various therapeutic properties depended upon one or the other of the several glucosides

occurring in the drug. More recent experience, however, has shown that the active principles of digitalis act primarily on the heart and blood-vessels, and all other effects are secondary; but in many cases the secondary action of the drug is undesirable.

Of the active principles of digitalis, digitoxin is by far the most important and possesses the heart-stimulating property to a much greater degree than any of the other principles.

The cardiac action of digitalis is its most important effect and one which has been studied very widely, particularly on the heart of the frog. The action of digitalis on the frog's heart is very characteristic. After administration it can be observed that the rhythm of the heart is slowed and that on contraction it occupies a smaller volume and does not dilate as fully as under normal conditions. The ventricle is observed to be whiter during contraction, and on dilation does not become so red. A tracing forms a plateau when the heart is in systole.

A frog killed by digitalis dies with its heart in systole. This happens very rarely, if at all, with the mammalian heart, and was thought for a long time to be a distinguishing feature between the action of digitalis on cold-blooded and warm-blooded animals. However, recent research shows that the changes which take place in a frog's heart under digitalis are very closely related to those taking place in the mammalian heart. We can divide the action of digitalis on the mammalian heart into three stages: First, the therapeutic stage, in which the rhythm of the heart is slowed and there is an increased and prolonged systole. The ventricles more nearly empty themselves of blood, and by their prolonged contraction maintain a higher blood-pressure in the vessels than normally. In the second stage, the rhythm of the heart and pulse is very slow and becomes irregular. During diastole the ventricles dilate more fully, while the systole is not so regular and many times weaker, so that more blood remains in the heart than before the drug was administered. This serves to distinguish the first and second stages; namely, in the first stage *more* blood is pumped out or expelled by the ventricle than normal; in the second stage, *less* blood is thrown out than normal.

The important clinical observation which distinguishes the one stage from the other is the irregularity of the pulse. When this occurs, the action of the drug is reaching the second stage and should be immediately withdrawn.

The third stage is the stage in which the toxic action of the drug is the most marked. In this stage the rhythm of the heart is markedly increased, sometimes the pulse is very much faster than normal, but the most characteristic feature of this stage is the extreme irregularity of the contraction of the ventricle. If we examine this by means of a tracing, we get a curve which is characterized by the extreme irregularity of the up-stroke, which represents the contraction of the ventricle. During this stage the effect of digitalis on the central nervous system is quite marked. Vomiting and convulsions are prominent symptoms. Death rapidly follows and is immediately preceded by an extreme irregularity and rapidity of the beat, the so-called "delirium cordis." On autopsy, the heart in mammals is found to be dilated and full of blood.

The first or therapeutic stage is the important one to consider in the administration of digitalis as a medicine. It has little, if any, relation to the second or third stage, and in fact any of the symptoms of the second and third stage are danger signals to be heeded, and call for the immediate withdrawal of the drug.

The question of physiological standardization of digitalis has resolved itself into the specific action of the drug on the heart of the frog. Frogs were treated with digitalis in varying quantities, and that amount of digitalis which would kill a frog of definite weight, and which on autopsy showed its heart to be in systole was considered to be an index of the physiological activity of the preparation.

While no objections can be offered against this method as showing one of the actions of digitalis on the heart, we do not think that it is an absolute or even a safe method for the standardization of this drug. It is, after all, only a toxic effect, and the fact that the frog dies with its heart in systole is not any more characteristic than the mammalian heart in diastole. In either case the animal dies, and the cause of its death is the action of digitalis on the heart, and this method of the physiological standardization of digitalis is nothing more than a determination of the lethal dose.

Recognizing the great irregularity of the frog in its response to digitalis, in which the season of the year plays a very important rôle, the difference with which different species of frogs respond to digitalis, and the necessity of carrying out tests on frogs of equal weight, it was deemed advisable to standardize digitalis by using a

mammal, particularly the guinea-pig, which is quite sensitive to digitalis and which does not appear to offer so wide a variation as is observed in testing this drug on frogs of different kinds and at different seasons of the year.

It was thought desirable also to determine what, if any, relation there was between the lethal dose of a digitalis preparation and the amount of digitoxin present, which principle is more easily determined by chemical means than the other principles accompanying it. The results of these experiments will be detailed in the second portion of the paper.

Experiments with various preparations of digitalis and with the active principle digitoxin point very clearly to the fact that digitoxin represents, if not all, by far the most important properties of digitalis.

In determining the lethal dose of any digitalis preparation, guinea-pigs are selected of 240 grammes weight. The preparation to be tested, if a tincture or fluidextract, is freed from the greater part of alcohol by evaporation at a low temperature and diluted with water to the desired quantity. Progressively increasing amounts are injected subcutaneously into the guinea-pig. A poisonous dose is followed within twenty minutes to a half hour by symptoms of excitement in the animal. The animal runs around its cage, trembles, and a very decided nausea is present. This is rapidly followed by convulsions, which rapidly increase in intensity and in the intervals between them. The animal usually dies during one of these convulsions. It has been observed after experiments on many animals that a dose of digitalis or its preparation which does not kill the animal within two hours is never fatal. This has been accepted arbitrarily as a standard, and that dose of digitalis which kills the guinea-pig of 240 grammes weight between an hour and a half and two hours after administration, we fix as our lethal dose. Upon determining the lethal dose of a given preparation by means of a series of guinea-pigs, we take the lethal dose so determined and administer that amount to five or six other pigs as a control. Without exception, we have found that the dose determined in a series invariably kills the same size pig under the same conditions.

How closely this lethal dose is related to the digitoxin present in a given preparation will also be shown in the second portion of the paper. Our work so far seems to justify us in using the toxic dose

determined for a warm-blooded animal as a control over the chemical assay rather than the commonly accepted method of standardizing digitalis by means of its action on the frog's heart.

The idea is rapidly gaining ground among clinicians that digitoxin is the real active principle of digitalis, from which all the effects of digitalis preparations can be obtained. Its use in a pure condition probably is a long way off, as no satisfactory preparations have yet been made available, and we must still depend for the most part on a reliable tincture or fluidextract for digitalis therapy; but as there are several other principles in digitalis other than digitoxin, which are not inert, but evidently reinforce digitoxin in its action, and as these principles are not easily determined by chemical assay, it seems advisable that digitalis should be standardized, as to digitoxin content, which assures us of its therapeutic effect and, furthermore, the toxic action of the combined principles should be determined by means of physiological test.

2. BY CHEMICAL MEANS.

BY CHARLES E. VANDERKLEED.

Both the title of the fourth paper on our programme this evening and the time at our disposal limit the scope of this contribution to a discussion of the *standardization* of digitalis preparations, and, therefore, to review the chemical work on this interesting drug, of such men as Homolle, Nativelle, Schmiedeberg and Keller, the monumental researches of Kiliani, or the more recent discussion of the latter with Cloetta in regard to his (Cloetta's) so-called amorphous digitoxin is uncalled for. Moreover, it is not yet possible to settle beyond all doubt the accuracy of the various chemical views about the digitalis glucosides that have been supported by the various investigators, although it is generally conceded that Kiliani's work affords us the most exhaustive and reliable data concerning this very interesting and, in part, very valuable substance. It may not be out of place, therefore, to endeavor to sum up briefly such facts as all are agreed upon in order to have before us a clear view of the digitalis standardization problem.

All authorities agree that digitalis leaves vary greatly in physiological activity, that those of the first year's growth are practically inactive, and that those only of the second year's growth, collected preferably at the commencement of flowering, should be employed.

Moreover, it has been shown not only that moist leaves quickly become worthless, and that only the dried, or almost completely dried, leaves can be kept for any appreciable length of time without deterioration, but that great care must be exercised in the process of drying, in order that the very process which is intended to aid in preserving the activity of the leaves be not instrumental in destroying it. (In Caeser and Loretz's report in the *Apotheker Zeitung*, 1907, p. 794, Dr. C. Focke is quoted as stating that to dry leaves until 1·5 per cent. moisture remains is a guarantee against deterioration. It is probable that this only means that when all but 1·5 per cent. of moisture has been removed, enough has been eliminated to guard against deterioration due to the hydrolyzing effect of the moisture, whereas, on the other hand, the drying has not been prolonged so far as to injure the delicate active principles.

It is perfectly apparent, therefore, that the appearance of the drug *per se* can be no criterion of its activity. The National Standard Dispensatory (page 530) states that there is no satisfactory method of distinguishing leaves of the first from those of the second year's growth. Moreover, the process of drying would serve further to render more difficult a macro- or microscopic distinction between active and inactive leaves, and the same sample of leaves, although originally good, but improperly dried, would be difficult to distinguish from the same lot when dried under proper restrictions as to heat and light. It has been my experience in examining samples of digitalis leaves for several years, that physical appearance is not a reliable criterion of quality, although the identity of the leaf can be established with comparative ease.

No one will deny, therefore, that some sort of standardization of digitalis leaves is not only highly desirable, but is indispensable to the putting of uniformly reliable preparations into the hands of physicians. Tested leaves only should be used for the preparation of infusion of digitalis to be used extemporaneously, and all preparations of digitalis intended to be kept for some time, such as the tincture and fluidextract, should themselves be subjected to some method of testing whereby not only proof of their activity, but its degree as well may be established. It is well recognized that the fact that tinctures and fluidextracts have been prepared from assayed drugs is not in itself a guarantee of uniformity.

The physiological action of digitalis is primarily that of a cardiac

tonic or stimulant, followed by a pronounced diuretic effect, as was brought out in the first portion of the paper. Assuming Kiliani's work to be the most nearly correct, we have present in digitalis leaves three principal glucosides—digitoxin, digitalin, and digitonin. Digitoxin is a crystalline glucoside, soluble in alcohol and chloroform and in a mixture of alcohol, glycerin and water, slightly soluble in ether and insoluble in water and petroleum benzine; digitalin is an amorphous glucoside, soluble in alcohol and in a mixture of alcohol and chloroform, but only sparingly soluble in ether, chloroform and water; while digitonin is a crystallizable glucoside, soluble in alcohol and in a mixture of alcohol and chloroform, but sparingly soluble in chloroform alone, and differing from the other glucosides in being somewhat more soluble in water. Moreover, this glucoside renders digitalin and possibly also digitoxin more soluble in water—this effect being retroactive on the digitonin, increasing its water solubility. This effect is probably further increased by other constituents of the leaves such as saponins. It is in this way that the activity of an infusion of good digitalis leaves is accounted for. In this connection I wish merely to mention some experiments in which we attempted to prepare a permanent aqueous solution of the digitalis glucosides directly from the drug, depending upon the permanence of this mutually reactive, increased water-solubility effect. They were unsuccessful, however, since, although fully active at first, they gradually deteriorated, until, after two or three months, scarcely a trace of heart-stimulating principles remained in solution. It is apparent, therefore, that only hydro-alcoholic preparations, or those in which part of the alcohol has been replaced by glycerin, will be practically permanent.

Of these three glucosides digitonin is present in greatest amount, but is devoid of all heart-stimulating action. Digitoxin is present in next to largest amount, while true digitalin comes last. Digitoxin is the substance which is by far the strongest heart-stimulating principle in the drug, although the true amorphous digitalin also possesses the heart-stimulating action to a marked degree.

Much of the confusion of prevalent ideas about the relative activity of the digitalis glucosides is due to the unfortunate jumble of names applied to them. Thus, commercial German digitalin, of variable activity, is composed principally of digitonin, while crystallized French digitalin is probably identical with digitoxin.

The difficulty of standardizing digitalis preparations, therefore, lies in the fact that no single constituent represents the entire physiologic effect of the drug. But this is not the only case of that kind—we have many drugs with which this condition exists, such, for example, as strychnine and brucine in nux vomica; and morphine, codeine, narcotine, etc., in opium. This fact has not deterred us from officially adopting an assay process for nux vomica, based upon the strychnine content; for opium, based upon the morphine percentage; and for cinchona, based upon the amounts of the alkaloids relatively more soluble in ether, namely: quinine, cinchonidine and quinidine. Why, then, should we not consider equally valuable an assay process for digitalis based upon the percentage of its most active heart-stimulating glucoside, digitoxin? May it not be that such a standardization of digitalis will prove to be quite as accurate and efficient as the standardization of cinchona bark, based upon the percentage of ether-soluble alkaloids which it contains?

The object of this joint paper is to throw light upon that question. We shall endeavor, by means of a table with parallel columns, to show that a fairly constant ratio exists between the chemical assay, *based upon the single constituent digitoxin*, and the result of the physiological test on standard guinea-pigs, which, of course, is that due to the combined effect of all of the active principles. It is not necessary that the constituent which is determined should possess the entire activity of the drug, nor is it claimed to be so in this case. It is only necessary that the amount of the readily determined principle bear a fairly constant ratio to the combined action of all of the drug constituents, in order to make such an assay process valuable. In this connection, however, Dr. Robert A. Hatcher states in the *Journal of the American Medical Association* for December 22, 1906, in referring to the digitalis glucosides, that "digitoxin more nearly represents the leaf," and that "despite the numerous disadvantages of digitoxin, it bids fair to displace digitalis in therapeutics." While I do not believe that Dr. Hatcher has given sufficient consideration to the great disadvantage of the insolubility of digitoxin in neutral media, thereby rendering its hypodermic use impossible, I fully agree with him in believing that digitoxin is by far the most important constituent of digitalis, and that it sufficiently nearly represents the drug to enable us to standardize the drug by means of it.

The physiological method of testing was described in the first portion of the paper. The chemical method for determination of digitoxin employed is essentially that of Keller, as outlined in Lyon's little book on the "Assay of Drugs," and is based upon the relative solubility of the digitalis glucosides in chloroform and water, depending for the final purification of the digitoxin from other principles on its complete insolubility in light petroleum benzine. The method, as used in our laboratory, is as follows:

Twenty grammes of the powdered leaves are exhausted by percolation with 70 per cent. alcohol, and the percolate is evaporated at low temperature on the water-bath until all alcohol has been dissipated (or if a tincture or fluidextract is to be tested, 200 c.c. of the former or 20 c.c. of the latter are taken and evaporated). The residue is diluted with or dissolved in sufficient water to make 150 c.c. Fifteen cubic centimeters of solution of lead subacetate (25 per cent.) is then added, and the mixture diluted to 200 c.c. The precipitate is filtered out and allowed to drain thoroughly, after which sufficient water is passed through the precipitate on the filter to insure saving all retained mother liquor. The united filtrates are again diluted to 200 c.c. and the excess of lead is precipitated by means of dried and powdered sodium sulphate or sodium phosphate.

After standing for twenty-four hours the precipitate is filtered out, allowed to drain well, and is then rinsed with water, in order to save all of the solution. (The taking of aliquot parts, thereby avoiding the necessity for completed filtrations and the washing of precipitates, cannot be recommended in digitalis assays on account of the vast bulk of the lead subacetate, sodium sulphate, or sodium phosphate precipitates.) The solution is transferred to a separatory funnel, 2 c.c. of 10 per cent. ammonia water added, and the mixture shaken out with five portions of chloroform of 30 c.c. each. The united chloroform solutions are evaporated to dryness on the water-bath in a tared flask and the residue of crude digitoxin redissolved in 3 c.c. of fresh chloroform. Ten cubic centimeters of ether and 70 c.c. of light petroleum benzine (the so-called 86°, which must leave no trace of residue on evaporation) are added and the flask allowed to stand in a cool place, covered by an inverted beaker for twenty-four hours. (In hot summer weather the flask is placed in a refrigerator.)

The digitoxin in micro-crystalline form will be found adhering to

the sides and bottom of the flask, from which most of the supernatant liquid can be decanted. The last few drops are evaporated and the residue dried to constant weight at 60° C. The weight of digitoxin so obtained, multiplied by five, will express the percentage present in the drug.

The following table shows the comparative results of a series of chemical and physiologic tests on the same preparations:

No.	Preparations	Chem. assay: grammes digitoxin in 100 c.c.	Physiologic assay: amount to kill 240 gramme pig in two hours
1.	U. S. P. tincture	0·0377	0·6 c.c.
2.	" "	0·023	1 to 1·25 c.c.
3.	" "	0·0277	0·75 c.c.
4.	" "	0·0254	1 c.c.
5.	Fat-free "	0·027	1 to 1·25 c.c.
6.	Fluidextract	0·264	0·1 c.c.
7.	" "	0·2405	0·09 to 0·1 c.c.
8.	" "	0·234	0·08 c.c.
9.	Powd. extract	(1·061 per cent.)	0·019 to 0·025 grammes.

It will be seen from the table that quite a uniform relationship exists between the percentage of digitoxin found and the amount of the preparation required to kill a standard-weight guinea-pig in a definite time. Taking any one of the preparations in the table as a starting-point, as the amount of digitoxin in column two increases, the amount of the preparation required to kill in the third column decreases, the amounts being inversely proportional. These results would lose much of their meaning and value if the preparations assayed had all been prepared from one lot of drug. Such, however, was not the case, as the experiment extended over a considerable period of time and covered several different shipments of digitalis leaves.

The fat-free tincture referred to in the above table is one prepared from drug which has first been exhausted with petroleum benzine to remove fats, volatile oil, etc., thereby making the preparation miscible with aqueous solutions without causing precipitation. This treatment has apparently little or no effect on either the chemical or physiological assay.

A summary of my records on the assay of digitalis leaves, going back about four years, shows the following facts:

Highest percentage of digitoxin	0·455 per cent.
Lowest " "	0·171 "
Average " "	0·313 "

In two experiments on the rate of deterioration of preparations of digitalis, one fluidextract lost in 17½ months 22·6 per cent. of its digitoxin, and another fluidextract in 25 months lost 15·9 per cent. These were preparations which came back to the laboratory after having been out in the trade, and we have no knowledge of the conditions as to light, heat, etc., under which they were kept during the time specified. These results would indicate, however, that under ordinary trade conditions fluidextract of digitalis deteriorates at the rate of about 11 per cent. per year.

RESEARCH LABORATORY OF THE
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NOTES ON COMPOUND RESORCINOL OINTMENT, N.F.

BY E. FULLERTON COOK, P.D.

This ointment has been the source of considerable discussion and some annoyance on the part of pharmacists throughout the country, owing to the difficulty which is experienced in preparing it when the N.F. directions are strictly followed. Resorcinol is described in the Pharmacopœia as "colorless needle-shaped crystals," etc., and the paragraph further states, "it acquires a pinkish tint on exposure to light and air."

Until very recently resorcinol, as found in the pharmacy, was a needle-shaped crystal corresponding to this description; consequently, in preparing this ointment, for which there has been considerable demand, it is necessary to finely powder the crystals in order to incorporate them in the wool-fat, as directed in the N.F. The experience has usually been that it is very difficult to obtain a smooth ointment at this point, owing to the difficulty of powdering the resorcinol. In fact, the water has a tendency to separate from the wool-fat, producing a spongy mass. This condition was experienced with an old sample of hydrous wool-fat, a sample newly purchased, and with one prepared by incorporating 30 per cent. of water with anhydrous wool-fat. The difficulty in incorporating resorcinol with the wool-fat may be overcome in one of two ways: either by obtaining resorcinol in an impalpable powder, which has recently been offered the trade, or by dissolving the crystal resorcinol in the

30 per cent. of water, which would normally be present in the hydrous wool-fat, and incorporating this solution with the right amount of warmed anhydrous wool-fat.

The next difficulty which confronts the manipulator is the addition of the melted paraffine and petrolatum to the mixture of resorcinol, zinc oxide, bismuth subnitrate, and hydrous wool-fat.

My experience at this point in the preparation of the ointment I find to be similar to many others. When this melted mixture of paraffine and petrolatum is added to the remainder of the ointment, whether it be in a mortar or on an ointment-slab, the paraffine will separate in small white particles, owing to its having a much higher melting-point than the petrolatum, and, consequently, cooling more quickly, and when this condition is experienced the usual remedy which the pharmacist adopts is that of rubbing small portions at a time until they are uniform. This involves much labor and the result, at best, is unsatisfactory. Having spoken with a number of pharmacists, I understand that this experience is common, and the strict following of the directions given in the N.F. for its preparation will, I believe, always be unsatisfactory.

After a number of experiments the following modification of the N.F. directions for preparing this ointment, without changing the ingredients, is offered: Dissolve the resorcinol (6 parts) in 10½ parts of water, with the aid of a little heat. Warm 24½ parts of anhydrous wool-fat contained in a porcelain dish on a water-bath, using just a sufficient amount of heat to soften the wool-fat, and add the solution of resorcinol, stirring continuously; then add the 6 parts of bismuth subnitrate and 6 parts of zinc oxide, continuing trituration until perfectly smooth. Having melted the paraffine and petrolatum together, add the mixture to the warmed wool-fat, to which the other ingredients have been added, stirring continuously. Finally, incorporate the 12 parts of oil of cade, and continue the stirring until the ointment is firm.

An ointment made in this way is perfectly smooth, and although the detail here given may seem unnecessary to those who have not tried this ointment, one experiment with each, which may require two hours of hard work to accomplish by the N.F. method, and fifteen minutes by the proposed method, resulting in a superior product, should convince the most skeptical of the need for a change in the N.F. directions.

One other point should be spoken of in connection with this ointment. It is directed in the N.F. that this ointment should be protected from light. The change of color which occurs is quite striking and is attributed usually to the resorcinol, which, as a phenol, becomes pinkish, as is recognized in the Pharmacopœia, when exposed to light and air. This change of color is undoubtedly due to the presence of this phenol, since the mixture of all the ingredients excepting the resorcinol will not show such a change, but, on the other hand, if the ointment be prepared to the point of adding the oil of cade, and this mixture allowed to stand, the creamy white color is not noticeably modified by exposure to either light or air for at least ten days. The conclusion which must be drawn is that the resorcinol and the oil of cade together are responsible for the color changes. To a sample of the ointment, completed, excepting the addition of the oil of cade, creosote was added. There is no change in color.

Acetic acid was added to another sample, likewise without affecting the color. It is evident that some other principle is present in the oil of cade to cause this rapid oxidation.

These color changes are quite striking. The ointment, when first prepared, is of a light, reddish-brown color. Within one-half hour it has changed to a gray-brown on the surface and inside of one hour it develops a distinct, pinkish tint. If this be exposed to light and air for twenty-four hours, it has assumed, on the surface, a purplish color, much darker than at first. This change seems to be due more to contact with air than to light, for the same change seems to occur in an ointment kept in a closed ointment jar, although the change is only upon the surface; the ointment one-eighth of an inch below the surface showing no purplish color, but the same gray-brown which it had assumed soon after preparation. It has been suggested that the ointment be prepared, excepting the addition of the oil of cade, and that the oil of cade be added when the ointment is dispensed. This, if followed, will insure a uniform product when the ointment leaves the pharmacy.

A GLANCE AT ANCIENT AND MODERN HINDU MEDICINE.

By Anna S. Kugler, M.D.

The claims made by the Hindus in regard to the antiquity of their medical science exceed those made by any other people. The Ayur Veda, or Science of Life, is considered to be a portion of the fourth or Atharva Veda. Brahma communicated the Ayur Veda to Dakshprajapati, who, in turn, communicated it to the Ashvini Kumars, the twin sons of the Sun.

The Ayur Veda consisted of one hundred adhyayas or sections, of one thousand slokas or stanzas each. It is divided into eight parts, as follows:

(1) Skalya (surgery). This includes the methods of removing foreign bodies, of using surgical instruments, of applying bandages, and of treating various surgical diseases.

(2) Shalakya. Treatment of diseases of parts above the clavicles or collar-bones, such as diseases of the eyes, nose, mouth, etc.

(3) Kaya Chikitsa. General diseases affecting the whole body, such as fever, diabetes, etc.

(4) Bhoot Vidya. Demoniacal diseases.

(5) Kanmara Bhritya. Management of children and diseases of mothers and nurses.

(6) Agada. Antidotes for poisons.

(7) Rasayana treats of medicines preserving vigor, restoring youth, improving memory, and curing and preventing diseases in general.

(8) Vajikarana. This treats of how the increase of the human race could best be promoted.

It is said that the oldest existing treatise on Indian medicine is that ascribed to a son of the Vedic Saint Atreya, and hence called the Atreya Samhita. This is a very large work, consisting of several divisions. Atreya is said to have met some of his pupils on the northern face of the Himalayas.

Harita, one of the pupils, asked questions on the origin and treatment of disease. Atreya explained that the Ayur Veda or Medical Science could not be fully explained within the limits of human life, and that his pupils must be content with his own composition, which is completed within 1,500 stanzas. These treat of almost all

varieties of diseases and prescribe remedies for the same. Diseases are classified as curable, incurable, curable by charms, and scarcely possible to be cured. The medicinal qualities of different kinds of water are explained; also of the different kinds of milk, and of the flesh of animals. One chapter treats of the moral causes of diseases. In another chapter diseases are treated of in detail. Intermittent fever is of four varieties, according as to whether it recurs in one day, three days, four days, or longer. Dysentery, diarrhœa, indigestion, consumption, etc., are discussed.

The two most highly revered and most frequently quoted of ancient medical writers among the Hindus are Charaka and Susruta. It is extremely difficult to arrive at a correct estimate of the date of these authors. According to some, Charaka lived 320 B. C. Professor Wilson, who is authority on many things in India, states that, as he is mentioned in the Puranas, he must have lived before the tenth century. Be that as it may, he was the greatest physician of his day, and his Charaka Samhita is still held to be a standard work on medicine. It was his desire to teach men to so manage their bodies as to avoid all unnecessary pain on earth and to ensure happiness after death. Charaka stated that he received the contents of his work indirectly from Atreya. Like that of Atreya, it is divided and subdivided, and covers a wide range in its consideration of the origin, nature and treatment of disease. One division treats of drugs which cause vomiting and purging, and six hundred remedies of this character are mentioned and classified according to the place they come from. Another division describes how medicines should be introduced into the body by means of syringes and tubes, and in what cases emetics, purgatives and enemas should not be used.

The work of Susruta is held in as high esteem by native vaichyas or physicians as an authority on surgery as is that of Charaka on medicine. The cause assigned for the meagerness of the surgical instruments and appliances of the ancients is that their acquaintance with the properties and virtues of drugs was so great that most of the diseases and injuries now dealt with by the surgeon were then cured by medication. An abscess was made to subside by plasters or brought to maturity by poultices. Cases of urinary calculi were treated by antilithics and diuretics. And yet in their works no less than 125 surgical instruments are described.

Hindus were experts in forming new ears and noses, owing to the punishment so common then in India of cutting off the nose and ears. Dr. Hirschfeld, of Berlin, is quoted as saying: "The whole plastic surgery of Europe took new flight when these cunning devices of Indian workmen became known to us. The transplanting of sensible skin-flaps is also an entirely Indian method." The Hindus are also credited with discovering the art of cataract couching.

In Cæsarean section and other abdominal operations, and in amputations, they are said to have been experts. Inoculation for smallpox is said to have been known to them at a very early date.

According to Dr. Wise, the Hindus were acquainted with practical anatomy, and Sir Bhagavat-Singh Jee says that they taught and practiced the dissection of the human body, but the consensus of opinion seems to be that anatomy was the weakest side of Indian medicine. The following method of studying the structure of the human body is given:

Let the physician have the corpse, together with its receptacle, fastened in a brook to macerate. At the end of seven days the corpse should be rubbed with pieces of bark and all the external and internal parts can then be seen.

The human body is said to consist of 6 members, the 4 extremities, the trunk and the head; and has 7 membranes, 7 segments, 70 vessels, 500 muscles, 900 sinews, 300 bones, 212 joints, 24 nerves, 9 organs of sense, etc. The vessels contain not only blood, but carry also bile, mucus and air.

Very explicit directions are given in regard to the surgeon and the way in which he is to acquire manual dexterity. He was to practice scission or cutting on flowers, incision on skins or bladders filled with paste, lancing on the hollow stalks of plants, sutures on skins, ligatures and bandages on well-made models of human limbs. Susruta directs that the surgeon, before commencing his art, should equip himself with all the requisites, such as the instruments, salts, bandages, honey, oil, water, etc. He should have practical experience in his art and should have seen many operations performed by others. He should be intelligent, steady and skilful, and should have a light hand. He should have steady and strong attendants to assist him. A certain incense should be kept burning in the operation-room. The surgeon should not leave his patient without

offering a prayer to the Almighty for his recovery. Should the wound cause intense pain, a cloth soaked in melted ghee and licorice may be applied. The operations were performed on auspicious days, and the patient was made to sit or stand with his face to the east.

In cases of patients dreading the knife, and of children, sharp pieces of bamboo or glass were substituted. Leeches, caustics, and hot charcoal were used in the treatment of certain affections. The surgical instruments were to be made of the best steel and kept in handsome portable wooden boxes. It is thought that the disappearance of surgery from Hindu medicine is chiefly due to the aversion of the Brahmins to touching a dead body, and to coming into contact with pus, blood, etc. Surgery thus passed from the priestly class into the hands of the lower classes, and for lack of encouragement declined altogether, until bleeding was left to the barbers, bone-setting to the herdsman, and the application of blisters to every man.

The obstetric art is considered a branch of surgery and is treated at great length. External circumstances were supposed to act very powerfully on the physical and moral qualities of the offspring. On this account the woman, from the time of conception, should be kept happy, should remain pure, and should wear ornaments and white clothes. She should not touch a dirty, diseased or imperfectly formed individual. Great attention should be paid to the diet: during the first three months the food should be very cool and thin, as rice and milk. When abortion is threatened, cold water and cold bathing should be used. On a favorable day in the ninth month the pregnant woman is to be removed to a temporary hut built for the purpose, the door to the east or south. Four experienced women should be selected to assist at delivery. Sour gruel in large quantities was to be given to assist in the expulsion of the fœtus. In case of delay the smoke of the skin of the black serpent was to be applied to the vagina.

When the infant was born, a little fine salt and ghee were mixed and put in the mouth, a mixture of linseed, margosa leaves, and ghee was rubbed upon its head, and a piece of oiled cloth put over it. The cord was tied eight fingers from the navel and then divided, and one end was tied around the neck to prevent evil. A little cold water was then thrown over its face, and the father offered up the

prescribed prayers. Much was written in regard to dystocia, and directions were given in regard to Cæsarean section.

The ancient Hindus paidgreat attention to hygiene and prescribed rules for the regulation of the life of the individual, both in sickness and in health. Health was thought to be promoted by the exhibition of an emetic once a fortnight, a purgative once a month, and blood-letting once a year.

Having thus briefly glanced at surgery, as practiced by Susruta and others, we return to the subject of medicine by giving a description of a good physician. He must be a person of strict veracity, of the greatest sobriety, of good moral character, and be versed in all the commentaries of the Ayur Veda. He must be a man of sense and benevolence, his heart must be charitable, his temper calm, and his constant study how to do good. He should daily improve his mind by an attentive perusal of scientific books. He should have his hair dressed and his nails pared; should have clean clothes and carry a stick. To treat a patient conscientiously was supposed to bring punyam or merit to the physician. For the sake of his livelihood he will be justified in expecting a fee from well-to-do people. The Hindus are enjoined not to approach a king, a preceptor or a physician empty-handed.

The Hindus were then, as they are now, very particular about the selection of auspicious days for the preparation of their medicines and the beginning of treatment. For instance, Mondays, Tuesdays and Saturdays were inauspicious days for certain drugs. Tuesdays, Thursdays and Sundays were the best days for the administration of purgatives and emetics.

In regard to prognosis, diseases were classified as curable (sadhya), incurable (asadhya), and controllable by remedies only (yapya). The physician is warned to refrain from treating a disease that is quite incurable.

They claimed that of all diseases the etiology was as follows: Adverse correlation, absence of correlation, and excessive correlation of time, mind and the organs of the senses. Time here means not only that which is divided into days, weeks, etc., but infancy, youth, manhood and old age. All morbid phenomena were attributed to the disordered condition of the three principal humors of the body, called doshas, viz.: wind, bile and phlegm. These three humors were supposed to fill the whole body, but the principal seat

of the wind is between the feet and the umbilicus, of the bile between the umbilicus and the heart, and of the phlegm, between the heart and the vertex. Wind predominates in old age, bile in middle life and phlegm in childhood.

The whole system of Hindu medicine centers around these three forces. These words do not have the same meaning attached to them in ordinary language, but are technical terms used to imply certain states of the body. Treatment is regarded as depending upon the physician, nurse, patient and drugs.

Omens played an important part in the mind of the Hindu physician. A few good omens were : an umbrella, cow with calf, woman with baby, two Brahmins, horse, elephant, dancing-girl, and full water-pot.

Among unlucky omens were grass, snake, raw cotton, oil, enemy, butter-milk, one-eyed person, crow, corpse, and empty water-pot.

The messenger sent to call the physician should be of the same sex and caste as the patient, of good breeding, clever, clean, well dressed, driving a horse or bullock, and holding fruits and white flowers in his hands. A widow or a beggar is not a suitable messenger. Importance was attached by the physician to the dreams of the patient. When other remedies failed, the horoscope was consulted. The duration of a disease was believed to be influenced by the day on which it manifested itself.

Among the causes of disease Karma or Fate took an important place. Thus, the murderer of a Brahmin suffered from anæmia, a cow killer from leprosy, etc. Diseases caused in this way may be cured by propitiatory rites, or if these fail, the progress of the disease will be checked in the life to come.

Demons also were recognized as agents in the causation of certain affections. Such diseases, as well as many others, were cured by amulets and charms.

In diagnosing disease, physical signs, such as palpation, percussion and auscultation, etc., were recognized and referred to in the work of Charaka. The materia medica of the Hindus was most elaborate, and in it were described the properties of drugs belonging to the animal, vegetable and mineral kingdoms. Charaka gives 50 groups of 10 herbs each, which he thought enough for the purpose of an ordinary physician.

Susruta arranged 760 herbs in 37 sets. Other writers classified

remedies as antispasmodic, cathartic, expectorant, diuretic, hypnotic, hydragogue, anæsthetic, etc.

In addition to Charaka and Susruta, there were many authors of note in ancient and medieval India. An oft-quoted Sanscrit stanza states that "Madhava is unrivaled in diagnosis, Vagbhatu in principles and practice of medicine, Susruta in surgery and Charaka in medicine."

During the palmy days of Buddhism in India, under the reign of Asoka, in the third century, priests associated themselves in companies for the education of children, the relief of the sick, and the propagation of the Buddhist religion. Hospitals were erected and a regular system of medical administration established throughout the kingdom. With the decline of Buddhism these institutions disappeared. We close this part of our subject with a quotation from Prof. Wilson: "The ancient Hindus attained as thorough a proficiency in medicine and surgery as any people whose acquisitions are recorded."

Several things combined to bring about a decline of Hindu medicine and surgery. Of these a very important one was the contempt with which the Mohammedan conquerors of Hindustan regarded the scientific knowledge of the Hindus. The diffusion of the European system of medicine also acted as a discouragement to the study of the Sanscrit works. As time went on the ancient works became more inaccessible, and imperfect copies were substituted. Thus confidence diminished and superstition and quackery increased.

Let us now turn to the condition of Hindu medicine as it exists in India to-day.

Of the native physicians of to-day, an experienced Hindu apothecary writes, that "most of the native doctors are those who, having failed in other spheres of life, adopt the healing profession as an easy means of getting a living." He also writes: "In villages where no English medical aid is available and where the patients are poor, they cannot but have recourse to native doctors. If the disease or complaint is an ordinary one, these poor people get well. If severe and complicated, they are sure to die by maltreatment. My belief is that those unfortunate beings who fall into the hands of native quacks are up to 50 or 60 per cent. killed by over-drugging or poisoning by aconite, arsenic or mercury." The description given by this gentleman is similar to my own experience.

In the bazaars of every large town in India will be found one or

more shops in which are kept for sale an assortment of English medicines, and native medicines are found in all the bazaars.

The ordinary native doctor, whose preparation consists in the purchase of a few bazaar drugs and the assumption of a knowledge he does not possess, often succeeds in making a very good living. Mercury is much used as a remedial agent, and it is not uncommon to see ankylosis of the jaw, necrosis of the maxillary bones, and gangrene of the cheek as the result of its use.

The actual cautery is much used, and a common way of applying it is by means of wicks dipped in boiling oil. Every newborn child is burned a number of times over the abdomen. Paralysis, convulsions, abdominal and pelvic disorders are treated with the actual cautery, and we often have patients brought to us covered with burns.

The superstitions of the people are taken advantage of by the native doctors. This is especially true in the case of the devil doctors. Many forms of nervous and mental diseases are believed to be the result of devil possession, and I have known of well-marked cases of hysteria, mania, etc., being treated as such. A few months before I left Guntur, I spent several hours with three devil doctors, two old men and their nephew. They had inherited the profession from their father, and would pass it down to their sons. They gave me a very elaborate account of their method of exorcising devils, the principal feature of which was the repetition of mantrums or prayers, which are composed of various combinations of sixty-four letters. After the devil has been exorcised the doctor ties a charm around the neck of the patient. Thurston, in his "Ethnographic Notes," devotes a large space to omens, evil eye, charms, etc.

Mantrams or consecrated formulas are considered so powerful that even the gods can be brought under control. They are efficacious in curing diseases, in protecting children against devils, and women against miscarriage. Many of the disorders of children are attributed to the evil eye. The following is one of the many remedies: Some chillies salt, human hair, nail-cuttings, and finely powdered earth from the pit of the doorpost are mixed together, whirled three times in front of the baby, and then thrown on the fire.

Votive offerings also occupy a large place in the thoughts of the people, and the temples are daily thronged with those who have come to fulfil vows made during illness or because illness has

been averted. The offering may be a beautiful little daughter who will be married to one of the temple gods and brought up to a life of shame. One lady in South India has devoted her life to the rescue of these little temple girls. The cholera and small-pox goddesses are held in great esteem by the masses. During the cholera epidemic, in 1906, a great sacrifice was made in Guntur to the goddess, and at such a time buffaloes, goats, and chickens are offered.

In addition to these irregular methods of treatment, there is what may be called the regular school of Hindu medicine, to which a small class of native doctors belong. I have frequently met some of these men in the homes of the people, and not infrequently they are in attendance upon the patient at the same time as myself. These men are not averse to being interrogated as to their training, methods of treatment, etc. They have acquired their knowledge from their fathers and grandfathers, and from books handed down in the family. These books have been written in modern times, but are based upon those of the ancients, Charaka, Susruta and others, but are greatly inferior to them. The practice of the regular Hindu physicians of to-day is based upon a false knowledge of anatomy and physiology, and upon erroneous theories as to the cause and nature of disease. They have never dissected, have never seen the inside of the human body, have no knowledge of the clinical thermometer, the stethoscope, the microscope, etc., have attended no medical schools, read no medical journals, and belong to no medical society. For them the human body is composed of 306 bones, 210 joints, 900 ligaments, 700 vessels, etc.

In the diagnosis of disease great stress is laid upon the pulse, which in the male must be felt in the right wrist, in the female in the left. Many explanations are given for this, one being that the blood-vessels are differently distributed in the two sexes. The character of the pulse is largely depended upon for determining the predominance of one or other of the three humors of the body. If the pulse feels like the creeping of a serpent or a leech, wind is predominant, if it be jumping like a frog, or similar to the flight of a crow, bile predominates. When it strikes the finger slowly and resembles the strutting of a peacock it shows that the phlegm is in excess. As the health of the individual depends upon the proper relation of these three humors, disease is the result of a want of correlation, and the treatment of disease consists in the restoration

of this disordered relation. The use of drugs is based upon this theory, and all remedies are considered with reference to their effects upon these three humors.

According to them, every substance, whether animal, vegetable, or mineral, possesses five properties, namely rasa, guna, veerya, vibaka, and prabhava, which may be interpreted as taste, virtue, power, consequence of action and inherent nature. Some of the remedies derived from the animal kingdom are the bone of a goat, the tooth of an elephant, milk, human milk in eye diseases (this is very common), goats' milk in phthisis, etc. Kasturi or musk and the venom of snakes are much in use. Urine is used both internally and externally. Among the minerals used are metals, salts, precious stones and clay. The process of purification of the metals is very long and tedious.

The application of remedies to the eye as counterirritants, and to the crown of the head, are among the favorite methods in use.

Caste to-day rules the medical as well as every other profession in India, and the practice of the native doctor is well expressed in the words of one who said to me: "We treat all castes, but in cases where we find it objectionable to feel the pulse, we get full particulars regarding urine, etc., and then give necessary treatment."

Surgery has entirely fallen into the hands of Mohammedans and barbers. A number of arms and legs have been amputated in our hospitals as the result of the bamboo splints applied by the barbers. Midwifery is entirely in the hands of the barber women, or, as they are called in Southern India, the mantrasani. These women always wash their hands after the delivery of their patient, and we have had hundreds of their victims come to us, sometimes too late for craniotomy to save the mother, sometimes suffering from acquired atresia of the vagina, or it may be with vesico-vaginal fistula and other injuries of the birth-canal.

Some of the more intelligent of the Orthodox Hindu doctors are recognizing the limitations that hinder their development, and are endeavoring to bring about a revival of the Ayur Vedic system of medicine. The late Maharajah of Mysore established a college wherein a complete training, according to the Ayur Vedic system, is available. This system is also taught in Calcutta, Benares, Bombay, Madras and other cities.

The oldest and largest of the two schools of this kind in Madras

is known as the Madras Ayur Vedic College, and is under the auspices of the Sri Kanyaka Paramesvari Charities. The course of study extends over three years. The works of Charaka, Susruta, Bahata and other Ayur Vedic writers are taught. Anatomy, physiology, materia medica, midwifery and hygiene are also taught by graduates of the English Medical College of Madras. The students who pass the required examinations receive diplomas stating that they are qualified physicians of the Ayur Vedic system. At present they have only a dispensary in connection with this school, but they hope soon to have a hospital. From 200 to 300 patients are treated daily at this dispensary. When in October, 1906, I visited this institution, the superintendent, Pandit D. Gopala Charlu, was most courteous in his attention and showed me everything of interest. In the waiting- and treatment-rooms there was nothing to distinguish them from the ordinary Government dispensary. The prescriptions are written in Sanscrit and compounded in the drug-room by the students. The drugs are obtained largely from Mysore and Malabar, but a few herbs are cultivated in the garden adjoining the building. Pills, powders, tinctures, honeys, waters, ointments and oils are upon the shelves of the drug-room. Arsenic, strychnine, nux vomica, lead, zinc, mercury, iron and gold are used in different forms. The superintendent belongs to an old family of Hindu physicians and is on very friendly terms with European members of the medical profession. He has made a special study of plague, and has a special remedy for it. He writes: "In the good old days, more than a thousand years ago, when several of the nations now held up as models of civilization were naked savages, fighting for existence with many of their more formidable enemies, the great medical men of India were grappling with this formidable disease." It is the ambition of the Pandit to have an Ayur Vedic dispensary in every district of the Madras Presidency.

In conclusion, we may ask: What is the condition of medicine in India to-day?

It seems to me that the condition of medicine is not unlike that of religion. There is the quackery that has arisen because of the decline of ancient Hindu medicine; a system based on hypocrisy and deception, succeeding in proportion to the superstition and ignorance of the people, having its counterpart in modern Hinduism, with its temples and priests. There are the comparatively few hered-

itary medical practitioners who are, I believe, in many instances honestly trying to practice the healing art by closely adhering to the medical teaching that has come down through the ages. corresponding in part to the so-called Orthodox Hindu who goes back to the Vedas for his religious teaching. There are those who, in the recently established Ayur Vedic schools, are trying to combine the ancient and the modern systems, corresponding to the Brahmo-Somaj and other reform societies.

And, lastly, there is the medical science that, by means of the English Government and the medical missionary, has come from the West, bringing with it much that is good, not a little of which has been received from the East, to which it is brought, something in the way that Christianity, though originating in the East, is now brought back from the West.

What will be the outcome of it all? As concerns religion, it is not my purpose to attempt an answer here. I know of no one who has attempted to answer, as regards medicine.

It seems not too much to hope that, as the years go by, more attention may be paid to Ayur Vedic medicine by all students of medicine, and that that which is good in it may be incorporated into a system which, being neither that of the East nor of the West, may be a universal system of medicine whose chief object shall be the amelioration of human suffering and the prevention of disease.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF THE MORE IMPORTANT ADVANCES IN PHARMACY AND MATERIA MEDICA.

By M. I. Wilbert,
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Food and drug legislation is again attracting the attention of all branches of the drug trade. This is due to the fact that in a number of States the Legislature is considering the enactment of laws more or less in harmony with the Federal Act of June 30, 1906.

The Federal law has been in operation long enough to demonstrate that it is a factor for the bringing about of better conditions, despite the fact that it comes far, very far, from correcting all of the abuses that it was expected to remedy.

The surmise that Congress would be tempted to modify or amend the Federal law at an early date appears to have been well founded, as at least several bills amending the Pure Food and Drugs Act are now pending in committee, though it is hoped they will be allowed to remain securely pigeonholed until the law has been sufficiently tested to demonstrate its shortcomings and needs.

One of the proposed amendments, introduced by Senator Gallinger, of New Hampshire, proposes to make the Homeopathic Pharmacopœia of the United States a drug standard of equal standing with the Pharmacopœia of the United States. Apart from the fact that legislation of this kind would appear to be introducing conflicting standards, it has been pointed out that the Homeopathic Pharmacopœia of the United States is but one of several homeopathic pharmacopœias that are now in use in this country, and that it is not generally recognized by homeopathic practitioners.

A bill that has been introduced in the House by Representative Mann, of Illinois, is designed to correct the abuse that has grown out of the form of guarantee that is now allowed on the label. Practically the same object is sought by a bill that has been introduced in the Senate by Senator Heyburn.

While it is true that the present style of guarantee has been abused to some extent, attention is being called to the fact that manufacturers and others have but recently accommodated themselves to the provisions of the Food and Drugs Act, and it would be a hardship to compel them to destroy their stock of labels, now on hand, and revise the form of guarantee to conform with the modification proposed by either of the proposed measures.

The U.S.P. and N.F. propaganda is attracting considerable attention in various parts of the country. Retail pharmacists appear to have been uniformly successful in calling the attention of physicians to the articles official in the Pharmacopœia and the National Formulary.

It has been pointed out repeatedly that if this propaganda is to meet with the continued success that it rightfully deserves, retail pharmacists must take cognizance of their own shortcomings, from a scientific point of view, and endeavor to meet the increased demands that will be made on them. They will also be required to recognize their sins of omission and commission in connection with the nostrum traffic, and correct at least many, if not all, of the abuses

that are now so manifest. This latter need appears to have been dwelt upon at some length at a joint meeting of retail druggists and physicians recently held in Chicago.

Another need that has manifested itself is the improvement of many of the preparations enumerated in the National Formulary, also a few, at least, of the preparations of the U.S.P. This need has been recognized by the several branches of the American Pharmaceutical Association, and a concerted attempt is now being made to institute investigations looking to the possible improvement of U.S.P. and N.F. formulas.

The Chicago branch has been particularly active in this line of work and a number of valuable suggestions have been brought forward by members of this branch.

Discouraging the Prescribing of Secret Remedies.—That the present move to discourage the use of secret remedies by physicians is attracting the attention of thinking men in all parts of the world is evidenced by the action of the British Columbia Medical Association. At the annual meeting, held in Victoria, B. C., this Association adopted resolutions deprecating the use and sale of patent medicines and the prescribing of proprietary remedies by physicians.

The British Columbia Medical Council was requested to communicate with all physicians in the province, drawing their attention to the undesirability of prescribing secret proprietary remedies. (*Phar. Jour.*, December 7, 1907, page 769.)

In England the British Pharmaceutical Codex is being made the basis of a concerted propaganda on the part of the pharmaceutical societies. This book, but recently published by the Pharmaceutical Society of Great Britain, presents many interesting possibilities that are well worth careful consideration on the part of American pharmacists.

Proprietary and Trade Names.—Among the many features of the British Pharmaceutical Codex, the treatment that has been accorded the admittedly complicated problem of proprietary and trade names is perhaps the most interesting. In this connection an attempt has been made to introduce short and euphonious names for the more lengthy chemical names for substances not protected by patents. Among the titles thus introduced to take the place of trade names we find:

Acetannin for tannigen.
Acetomorphine hydrochloride for heroin hydrochloride.
Acid salaceticum for aspirin.
Adrenine for adrenalin.
Benzylmorphine hydrochloride for peronin.
Betacaine hydrochloride for β-eucain.
Chloramide for chloralamid.
Chlorbutol for chloretone.
Ethylmorphine hydrochloride for dionin.
Formamine for urotropine, and many others.
Formamol for citramin, helmitol and others.
Malourea for veronal.
Quinalgen for analgen.

These are but a few of the many new titles that have been introduced and serve to indicate the effort that has been made to introduce short, easily remembered names for articles sold under proprietary names. While it is true that many of these titles are open to criticism, it does appear as though the move is one to be commended as being a step in the right direction.

Sunday Rest.—In Prussia the apothecaries appear to have succeeded in their efforts to secure a whole, or at least a partial, day of rest on Sunday. A recent circular order sent out by the Prussian Government not alone permits, but actually provides for the introduction of increased facilities for Sunday rest on the part of pharmacists and their employees. In places where there are several pharmacies, Sunday closing is to be achieved by mutual agreement among the several proprietors, while in places with but one pharmacy, the police authorities are permitted to arrange for restricted hours. (*Chem. and Drug.*, January 4, 1908, p. 8.)

Origin of Titles.—According to Le Clere's famous "History of Medicine," the term Apotheke was first used to describe the storehouses of the herbalists. These traders were called Rhizotomoi and Botanologi by the Greeks, and Herbarii in Latin.

The title Pharmaceutes and Pharmacopes originally meant dealers in medicaments and became terms of reproach because of their dealing in poisons, love-philters and the various quackeries of the day.

In Rome the business was still more divided. Besides the herbalists, there were shops for medicaments, others for perfumes, others

for colors; curiously enough it was the Pigmentarii who seem to have been the most respected, and who ultimately absorbed the trade of the others. (*Chem. and Drug.*, December 28, 1907, page 968.)

Pill Excipient for Oxidizable Substances.—Pills of readily decomposed chemicals, such as silver nitrate, potassium permanganate, gold chloride and mercuric iodide, are readily massed by the aid of two parts of kaolin and one part of dried sodium sulphate with sufficient water to moisten.

The mass must be carefully and rapidly mixed and rolled out without delay, as it remains plastic only for a short time. The pills are said to dissolve much more readily than pills made with kaolin alone. (*Pharm. Zeit'g*, December 21, 1907, page 1059.)

The Lumière Process of Color Photography.—For many years experimenters have sought for a simple and readily followed method for fixing color by photographic means. A number of more or less complicated processes have been worked out, but it has remained for the Messrs. August and Louis Lumière to simplify the process so that it is now possible to produce photographs containing all of the shades and colors of the original, true to nature.

The Lumière process is, in fact, a practical application of the well-known three-color processes, and consists essentially of a screen containing the color elements, orange, green and violet, in the form of finely divided particles, spread evenly over the surface of a specially sensitized plate. These colored particles, with the addition of an equalizing screen, are utilized to act as a color screen in the taking of the picture, and serve to reproduce the color of the original object when the resulting picture is projected on a screen or viewed by transmitted light.

So far it has been possible to produce the pictures only in the form of glass positives, one at a time. Even this offers a wide field of usefulness, as the resulting pictures can be utilized as transparencies, or as lantern slides, and promise to be of great educational value.

β-Barbaloin.—Leger has succeeded in transforming barbaloin into an isomeric substance which he terms β-barbaloin. This isomeric aloin also occurs naturally in various species of aloes.

β-Barbaloin is uncrystallizable, but yields a crystalline chloro-derivative. Leger has identified β-barbaloin in Cape aloes and in

Uganda aloes, but only the merest traces of it exist naturally in Barbadoes aloes or other aloes rich in crystallizable aloins. (*Chem. and Drug.*, January 11, 1908, page 48, from *Jour. de Pharm. et de Chem.*)

Estimation of Eucalyptol in Oil of Eucalyptus.—Schimmel & Co., in their semi-annual report, for October 1907, give the following easily applied method for estimating the amount of eucalyptol in oil of eucalyptus:

"Ten cubic centimeters of the oil containing eucalyptol are mixed in a cassia flask of 100 c.c. capacity with so much of a 50 per cent. resorcinol solution that the flask is filled for about four-fifths of its capacity. The mixture is then thoroughly shaken for five minutes, and the oil portions which have not entered into reaction are brought into the neck of the flask by adding resorcinol solution, and their volume determined. By subtracting this volume from ten, the eucalyptol content of the oil is obtained; this is then expressed in percent. by volume by multiplying by ten."

Oils very rich in eucalyptol are suitably diluted beforehand with an equal volume of turpentine oil, as otherwise the eucalyptol resorcinol might crystallize out and cause the whole liquid to solidify.

Determination of Eucalyptol.—C. T. Bennett has experimented with the resorcinol method for the determination of eucalyptol in oil of eucalyptus, and finds that it gives results that are quite misleading. Bennett finds that the use of resorcinol solution gives results that are from 25 to 50 per cent. too high. The process of estimation given in the United States Pharmacopœia, on the other hand, Bennett finds, gives results that are invariably too low. (*Chem. and Drug.*, January 11, 1908, page 55).

Eucerine.—Unna claims that wool-fat does not owe its power of absorbing water to its cholesterin ethers, as stated by Dietrich, but to its free cholesterin and oxycholesterins; the oxycholesterins and their derivatives are free from odor and are unalterable, while the odor and gradual hardening of wool-fat is due to the cholesterin group of bodies. Unna has separated the oxycholesterin group of bodies and terms a mixture of 5 per cent. of them with 95 per cent. of paraffin, anhydrous eucerine, mixed with its own weight of water. This is eucerine, which is claimed to be an ideal ointment base for the exhibition of numerous substances that are to be absorbed. (*Chem. and Drug.*, January 11, 1908, page 48.)

Cacaosin is the name given to a substitute for oil of theobroma that is now being marketed in Germany. The substance has a melting-point of 28·5 and a congealing-point of 26·6, and is said to be admirably adapted as a vehicle and base for suppositories. It is probably a mixture of cocoanut oil with fats of a higher melting-point. (*Pharm. Zent'h.*, 1908, page 86.)

Constituents of Kola Seeds.—Perrot and Goris, in a critical review of the constituents of kola seeds, conclude that only three well-defined bodies have been isolated from this drug; caffeine, theobromine and kolatin. The last-named substance has been obtained from fresh seeds in small, white crystals that are slightly soluble in water, readily soluble in alcohol, acetone and acetic ether. (*Pharm. Jour.*, January 11, 1908, page 31, from *Bull. des Sci. Pharm.*)

Chinosol.—The Council on Pharmacy and Chemistry of the American Medical Association, in a recent report (*Jour. A.M.A.*, January 25, 1908, page 293) calls renewed attention to the fact that this article has been studied in Germany and found to be quite as poisonous for rabbits as lysol, and when given subcutaneously it is 100 per cent. more poisonous, but when absorbed from the peritoneum it is 50 per cent. less poisonous. While it is admitted to possess considerable antiseptic action, it was found to be decidedly deficient as a disinfectant.

The chemical composition of chinosol also varies from the claims that are made for it by the manufacturers and the American agents, who assert it to be potassium oxychinoline sulphonate. Chemical examination appears to indicate that it is really a simple mixture of potassium sulphate and oxychinolin sulphate.

Alexipon.—This is acetylsalicylic acid ethyl ester and has been recommended as an antirheumatic (*Phar. Zeit'g*, January, 1, 1908, page 9).

Borovertin is the trade name for a combination formed by the reaction of 1 molecule of hexamethylenamine on 3 molecules of boric acid, resulting in the liberation of 3 molecules of water, the conversion of the boric acid into metaboric acid and the combination of the latter with the hexamethylenamine.

The trade article occurs as a white, slightly acid powder, having a salty taste. It is soluble in 11 parts of water and in 48 parts of 96 per cent. alcohol. The composition is readily decomposed by heating. (*Pharm. Zent'h.*, 1907, page 941.)

Ferrated Milk.—Dr. Schmitgen (*Ber. klin. Wochenschr.*, 1907, page 1902), asserts that milk containing an unusually high percentage of true organic iron may be obtained from cows that are fed on specially prepared dry fodder containing readily absorbable iron compounds. This milk does not differ materially from ordinary milk but is said to contain from three to eleven times the amount of iron that is usually found in milk, and is said to be advantageous in the treatment of various forms of anemia. (*Pharm. Zent'h.*, 1907, page 1014.)

Ferroplasma is said to be an organic iron compound, extracted from cultivated plants of *Rumex crispus* (*Pharm. Zent'h.*, 1907, page 1014). In Merck's report for 1906 it is asserted that the roots of *Rumex crispus* have the faculty of absorbing considerable quantities of iron when grown on soil containing iron compounds.

Guaiodol.—This is an iodine derivative of guaiacol. Each guaiacol molecule is said to contain one atom of iodine and one free hydroxyl group, so that the preparation represents approximately 50 per cent. of iodine. It is said to be useful in all diseases of a tubercular nature. (*Pharm. Zent'h.*, 1907, page 1060.)

Hetraline, dioxybenzol hexamethylenetetramine, is being introduced into England as an intestinal antiseptic, particularly for the urinary tract. It is said to represent 60 per cent. of hexamethylenetetramine in true chemical combination with resorcinol.

Hetraline crystallizes in perfectly stable, snow-white needles that are soluble in 4 parts of hot water, or in 14 parts of cold water. It may be given in doses of 0·5 gm. (7 = ½ gr). (*Pharm. Jour.*, January 11, 1908, page 44.)

Hydropyrin.—Acetylsalicylate of sodium is being introduced in Austria as a substitute for acetylsalicylic acid. It is said to have the advantage of being freely soluble in water. (*Pharm. Zeit'g*, 1907, page 1051.)

Jute and jute seeds, according to Kobert (*Münch. med. Wochenschr.*, 1907, page 1143), contain a glucoside, corchorin, that is ten times as bitter as quinine. The lethal dose per kilo of animal, hypodermically, is 0·2 mg. for rabbits, 0·8 mg. for dogs and 2·9 mg. for horses. The toad is said to be singularly immune to the action of this poison, being 100 times less susceptible to its action than the frog. In the latter animal the drug slows the heart-beat and causes a systolic paralysis of the ventricle.

Corchorin belongs to the digitalis group of medicaments and is closely related to andromedotoxin.

Metadinitrobenzol as a Reagent for Sugar.—The reagent consists of 1 gm. of metadinitrobenzol dissolved in 100 c.c. of alcohol and 35 c.c. of a 33 per cent. soda solution; 10 c.c. of this solution, when mixed with a 1 per cent. solution of maltose, dextrose, lactose, galactose or arabinose gives a violet color in one minute, and with levulose in two minutes. Saccharose and glycogen produce no color. Aldehydes and ketones produce a red color and albumen, albumose, amido-acids, urea and keratin give a yellow coloration. (*Pharm. Zent'h.*, 1907, page 994).

Methylencitrylsalicylic acid is said to be produced by interaction between salicylic acid or salicylates and the dihalogens of methylencitric acid. The resulting substance is tasteless and nonirritating, and in this respect is said to be superior to acetylsalicylic acid. It is decomposed in the alkaline secretions of the intestines, liberating, in addition to salicylic acid, a small proportion of formaldehyde. It is said to be particularly useful in cases of rheumatism. (*Pharm. Zent'h.*, 1907, page 956.)

Morphine-brom methylate is produced by treating morphine with dimethyl sulphate, dissolving the resulting addition product in water and converting the same with a saturated solution of potassium bromide, which also acts as a precipitant for the resulting morphin-brom-methylate. The latter is then purified by recrystallizing from a solution in warm water. Morphin-brom-methylate occurs as white, needle-shaped crystals that decompose and melt at from 265° to 266° C.

It is readily soluble in hot water, and at 15° C. is soluble in the proportion of 1 in 20 of water. It is but slightly or not at all soluble in alcohol, ether or chloroform. Its uses are the same as morphine. (*Pharm. Zent'h.*, 1907, page 960.)

Paralysol is the name given to a cresol soap preparation that is being marketed in the form of tablets.

F. Zernik has recently examined these tablets and found them to consist, in round numbers, essentially of 75 per cent. of equal parts of m- and p-cresol in the form of a double salt of potassium, 15 per cent. of a soda soap, and 10 per cent. of talc and bolus. (*Apothek. Zeit'g*, 1907, page 1126.)

Pyrenol, a substance that was claimed to be benzoyl-thymol-

sodium-benzoyl-oxybenzoate, was examined by F. Zernik, at the Pharmaceutical Institute of the University of Berlin, and found to consist essentially of a mixture of 49·48 parts of sodium benzoate and 49·02 parts of sodium salicylate with 0·2 per cent. of thymol. (*Apothek. Zeit'g*, 1907, page 1091.)

Resorbol is said to be a combination of iodine with some of the higher fatty acids in the form of organic salts that are readily absorbed. It occurs as a brown liquid containing 10 per cent. of iodine in combination, but no free iodine. Resorbol has a specific gravity of 1·072 and mixes readily with water or alcohol in all proportions. It does not stain the hands or the clothing and is readily removed by washing. Resorbol has been used with reputed good results in cases of sciatica, neuritis and inflammation. (*Pharm. Zent'h.*, 1907, page 858.)

Solandrine.—Dr. J. M. Petrie has communicated to the Linnean Society of New South Wales an account of an alkaloid from *Solandra lævis* to which he gives the name solandrine. This alkaloid belongs to the atropin group and resembles hyoscine, but differs from it and its aurochloride in not reddening litmus phenolphthalein and in yielding atropic acid instead of tropic acid when hydrolyzed. The exact constitution of the alkaloid has not been worked out, but the results so far obtained appear to indicate the existence of a tropeine alkaloid in the plant. (*Chem. and Drug.*, January 4, 1908, page 14.)

Spirosol is the monoglycolester of salicylic acid and occurs as an oily, nearly odorless and tasteless fluid that is readily soluble in alcohol, ether, chloroform and benzol, and in about 110 parts of water. It boils at from 169° to 170° C.

Spirosol has been recommended to be used as a local application in cases of rheumatism, and is also said to be useful in cases of objectionable perspiration. It is claimed to be quite free from irritating effects and to be readily absorbed. (*Pharm. Zent'h.*, 1907, page 868.)

Synthetic Suprarenine.—This is said to be prepared by condensing catechol with chloracetic acid to form chloracetyl catechol, which is then treated with methylamine and the resulting methylamine acetyl catechol is reduced to dihydroxyphenylmethylaminomethylcarbinol, or synthetic suprarenine, which, in the form of the hydrochloride, is said to be indistinguishable, in physiological action, from the natural alkaloid of the suprarenal gland. (*Chem. and Drug.*, January 11, 1908, page 48.)

BOOK REVIEWS.

KURZES LEHRBUCH DER ORGANISCHEN CHEMIE. Von William A. Noyes, Professor of Chemistry in the University of Illinois. Translated by Walter Ostwald, and with a Preface by Wilhelm Ostwald. Leipzig: Akademische Verlagsgesellschaft m. b. H., 1907.

It can hardly be denied that our institutions of learning have not accorded to pure organic chemistry the prominent place this subject occupies in the German Universities, nor that the American contributions to its literature, both in text-books and original memoirs, will bear no comparison with the output of the German chemists. It might seem, therefore, like carrying coals to Newcastle to translate into German an American text on organic chemistry; and yet this has been done repeatedly and successfully. The present translation was made at the suggestion and under the direction of Professor Ostwald, who recognizes "the independent and original manner in which the author has conceived and solved his problem," as well as the fact that the modern developments of physical chemistry are adequately brought out by the author. As the book was first published five years ago, it seems unnecessary here to call special attention to its lucid style and logical arrangement, nor to the truly scientific spirit that pervades it. The German version leaves nothing to be desired; it reads like an original, and embodies a number of changes that enhance its usefulness to German students, as well as many additions and corrections supplied by the author. The type, printing and paper are decidedly superior to those used in the making of the American book; the cuts, however, are not up to the standard set by the best German and French text-books.

If the novel arrangement of the subject matter appeals to other German teachers as it did to Professor Ostwald, this translation may become even more popular than the original.

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PHARMACEUTICAL AND CHEMICAL PROBLEMS AND EXERCISES WITH EXPLANATORY TEXT, including pharmaceutical and chemical arithmetic, weights and measures, specific density and specific volume and chemical notation and nomenclature, chemical equations, problems in oxidation and reduction and stoechiometry, together with

the elementary theoretical chemistry necessary to their understanding. Intended as an aid to students, teachers and examiners. By Oscar Oldberg. Fourth edition, revised and enlarged. Chicago: Chicago Medical Book Company. Price, $3.00.

With the appearance of several books on pharmaceutical arithmetic, it is becoming apparent that a comparatively small proportion of the students of pharmacy have been grounded in the fundamental principles of arithmetic, or have devoted themselves to the mastery of these principles to the extent of being able to apply them with certainty in solving the every-day problems of the laboratory and prescription counter. This is not the place to discuss the question as to why this deficiency in the pharmaceutical student's education exists, nor to consider the ways for remedying this defect. Certain it is that books of the character of this one, by Professor Oldberg, are always welcome to both students of pharmacy and pharmacists, and when the subject is elaborated and presented so systematically, as in the present instance, it rises to the dignity of a distinct branch and presents a legitimate claim to a place in our curriculum.

The book contains two excellent chapters, of about 45 pages each, devoted to the review of elementary arithmetic (including fractions, reciprocals of numbers and their uses, proportion, percentage and alligation), and elementary theoretical chemistry.

The chapters on weights and measures, and solutions and mixtures, supplemented as they are by miscellaneous examples in proportion and percentage, are of particular value to the retail pharmacist. Teachers and the examiners on boards of pharmacy will find not only in the problems, but also in the text, a large amount of material that will be helpful in framing practical questions.

The problems and exercises relating to chemistry are equally well presented, and the chapters on the periodic system, chemical notation, oxidation and reduction, stoechiometry, are specially commended for the manner in which they are written. Part VI treats of specific density and specific volume, and will be found of great practical value, containing, as it does, a large number of miscellaneous problems on the relation of weight and volume, and rules for reducing Baumé degrees to specific gravity and vice versa.

Professor Oldberg's book is the best one we have seen relating to pharmaceutical and chemical problems, and should be in every laboratory and on the dispensing counter of every pharmacist, for use at a moment's notice.

A MANUAL OF MATERIA MEDICA, especially designed for students of pharmacy. By Prof. Edsel A. Ruddiman. Philadelphia and New York: Lea Brothers & Co., 1907. Cloth, $2.25.

The purpose of this book is set forth in the following statement taken from the preface: "In the multiplicity of books treating of the various phases of materia medica, there seems to be a place for one especially condensed and written for the student of pharmacy. The author has attempted to present, in as few words as possible, the work usually given to such students." While one may present the essential principles of a subject in a condensed form, or present an elementary treatise on a given subject, this is not the time to provide short cuts and quick turns for pharmacy students. On the other hand, the aim should be to inculcate the principles in each branch as thoroughly as possible, and at the same time to broaden the student's grasp of the subject.

Professor Ruddiman's Manual bears evidence that he was especially guided in his selection of material by the U. S. Pharmacopœia, Hare's Therapeutics, and Culbreth's Materia Medica. One wonders why, in a book of this kind, which is presumably written for students supposed to have a good preliminary training, weights and measures given in grains and inches are prominently brought forward, while the metric equivalents are given in parentheses, contrary both to the spirit and language of the Pharmacopœia, when apparently the latter was the source of the data given in all cases. The condensed treatment of the subject of constituents is unfortunate, so far as pharmacy students are concerned. This is the feature that should have been extended rather than that on the action and uses of drugs.

The reviewer believes that thoroughness and efficiency should be made the watchwords in the training of pharmaceutical students, and he uses this occasion to put pharmaceutical teachers and authors on their guard, lest they unduly condense and shorten the matter presented to their students.

PRESCRIPTION PRACTICE AND GENERAL DISPENSING. An elementary treatise for students of pharmacy. By Prof. J. H. Beal, 1908.

In the preface Professor Beal states that "the principal object of the following pages is to afford an outline of a systematic course of study for the novice in extemporaneous compounding, and is not

intended as a general treatise or handbook for the experienced practitioner." A question may be raised as to what the author means by "the novice in extemporaneous compounding." If he means one who has not had a prescribed course of training and study, then there is a possibility of the book's doing more harm than good, for such an one should not be permitted to engage in that most responsible of all the work which the pharmacist has to do, namely, extemporaneous compounding. If, however, he means the recent graduate of pharmacy, then the book does not fill a real want, for the graduate of pharmacy will supposedly be able to use the "general treatise" or "handbook," to which reference has been made. The book contains some good things, but why the author should have chosen this method of presenting them at this time is not clear, particularly when there are so many excellent books which the beginner, as well as the pharmacist, should have.

PHILADELPHIA MEDICAL SCHOOLS AND THE UNITED STATES PHARMACOPŒIA.

At an informal conference, called by Prof. Joseph P. Remington, of the teachers named below, in the medical schools of Philadelphia, the following resolution was passed:

"Resolved, that it is of the utmost importance for accuracy in prescribing, and in the treatment of disease, that students of Medicine be instructed fully as to those portions of the United States Pharmacopœia which are of value to the practitioner, and that members of the Medical profession be urged to prescribe the preparations of that publication, and further, that this resolution be forwarded to the Medical and Pharmaceutical Journals, and to the teachers of Medicine and Therapeutics in the United States."

James Tyson, John H. Musser, John Marshall, Horatio C. Wood, Jr., H. A. Hare, J. W. Holland, Alfred Stengel, David L. Edsall, Seneca Egbert, M. C. Thrush, James Wilson, E. Q. Thornton, John V. Shoemaker, I. Newton Snively, J. M. Anders, S. Solis Cohen.

February 3d, 1908.

PHARMACEUTICAL MEETINGS.

JANUARY

The stated Pharmaceutical Meeting of the Philadelphia College of Pharmacy was held Tuesday, January 21, at 3 o'clock, with Warren H. Poley, a member of the Board of Trustees, in the chair. A number of practical points were brought out in the discussion of the various topics on the programme which would consume too much space to record, but which emphasize the advisability of attendance by those who desire to profit from the discussions.

Mr. Joseph W. England read a paper on the "Comparative Composition of Milks," which was published in the February number of this JOURNAL, p. 55.

Dr. Horatio C. Wood, Jr. exhibited a modified Soxhlet apparatus (see page 106).

Dr. Wood also read a paper having the title, "Does Digitoxin Represent the Therapeutic Virtues of Digitalis?" (see page 107).

Mr. England said that he had reached the same conclusion as Dr. Wood, namely, that digitoxin is not wholly representative of digitalis, which was based on its chemical behavior. He referred to the insolubility of digitoxin, and thought that in view of this property it is probably not present in the infusion of digitalis.

Dr. C. B. Lowe enumerated the more important constituents of digitalis, giving their solubilities and therapeutic properties. He said that the infusion of the drug contains certain principles which render it valuable as a diuretic, and condemned the practice of preparing the infusion from the fluidextract.

With regard to the solubility of digitoxin, Mr. Chas. E. Vanderkleed stated when extracts of digitalis are made, the digitoxin is extracted along with other constituents, and that during the course of assay, according to the Keller method, it exists in solution, being present in the lead subacetate solution, from which, however, it separates out in the course of two or three months, and will not again dissolve.

Mr. M. I. Wilbert referred to German digitalin, which is a mixture containing some digitoxin, and said that the digitoxin is rendered soluble by the other substances present, and expressed the opinion that by reason of the presence of the associated principles there is probably some digitoxin in the infusion of digitalis.

In answer to a question by Mr. Vanderkleed, as to whether it would be practicable to standardize digitalis preparations on the basis of the digitoxin content, Dr. Wood gave a negative reply, and said that some years ago he had come to the conclusion that digitalin probably represents the drug better.

Dr. E. D. Reed said that Dr. Wood's experiments and his own did not wholly agree. He said that the cumulative action of digitoxin is very pronounced, and stated that when a toxic or one-third toxic dose of digitoxin is given to a dog, and followed in twelve hours by a similar dose, it will cause the death of the dog, the result being attributed to the cumulative action. Dr. Reed said that probably the association of the digitoxin with other principles in preparations was an advantage, but claimed that the therapeutic effects on blood-pressure and diuresis were due to digitoxin. While making the further claim that where so much confusion exists we are warranted in considering digitoxin as the most important constituent of digitalis, Dr. Reed said that we are not warranted in saying that digitoxin is as valuable as the preparations, namely, the fluidextract and tincture, due to its physical condition in these preparations, and perhaps to a slight action of the other constituents.

J. T. Harbold, apothecary at the Pennsylvania Hospital, said that the physicians at the hospital manifest more satisfaction with the tincture of digitalis than with digitoxin.

Mr. Poley stated that according to his observation the infusion is being prescribed more than the tincture.

Prof. E. Fullerton Cook gave some "Notes on Compound Resorcinol Ointment, N.F.," and demonstrated an improved method for its preparation (see page 120).

In discussing the paper, Mr. F. M. Apple said that owing to the small quantity of the salts, his practice was to mix the bases and to add the correct proportion of the salts at the time of dispensing the ointment.

Mr. Aquila Hoch stated that he had found that when white petrolatum was used in the preparation of the ointment, the color changed in a less degree, due probably to the lesser proportion of sulphur compounds which would react with the zinc salts.

Edgar R. Buzzell, a student of the college, read a paper on "Glycerite of Bismuth, N.F.," and F. S. Bonnell, also a student, read a paper on "Antiseptic Solution, U.S.P., and Alkaline Anti-

septic Solution," in which he called attention to the variation in the finished products, due to the difference in character of the essential oils used.

This group of papers was further discussed by the chairman, W. L. Cliffe, Ambrose Hunsberger, C. E. Vanderkleed, M. I. Wilbert, and Harry Martin.

In this connection Mr. Wilbert demonstrated a method for incorporating resinous solutions with aqueous solutions, which was originated by Valentine Smith, a German. It consists in adding the alcoholic solution slowly to the aqueous solution contained in a bottle, and then revolving the bottle very slowly, holding it in a horizontal position.

William McIntyre, chairman of the Committee on Special Schools of the Board of Education of Philadelphia, read an interesting paper entitled: "The Public School Gardens of Philadelphia."

Prof. Henry Kraemer called attention to a series of back volumes of the AMERICAN JOURNAL OF PHARMACY, a copy of the 1830 edition of the U. S. Pharmacopœia, and a copy of "Wegweiser," which had been presented by Mr. Jacob Eppstein, a local apothecary, whereupon a vote of thanks was tendered Mr. Eppstein.

FEBRUARY

The meeting for February was held on Tuesday evening, February 18th, with Dr. Adolph W. Miller, corresponding Secretary of the College, in the chair.

The meeting was devoted to an illustrated lecture on "A Glance at Ancient and Modern Hindu Medicine" by Anna S. Kugler, M.D. (see page 123). Dr. Kugler is a graduate of the Woman's Medical College of Pennsylvania, and has just completed twenty-five years of medical practice at Guntur, India, where, under the auspices of the General Synod of the Lutheran Church, she has helped to establish a large hospital for women.

Dr. Kugler's paper, as here published, is an abstract of two papers prepared in 1905 and 1906 for the Oriental Society of the American Evangelical Lutheran Mission, Guntur, India.

FLORENCE YAPLE,
Secretary pro tem.